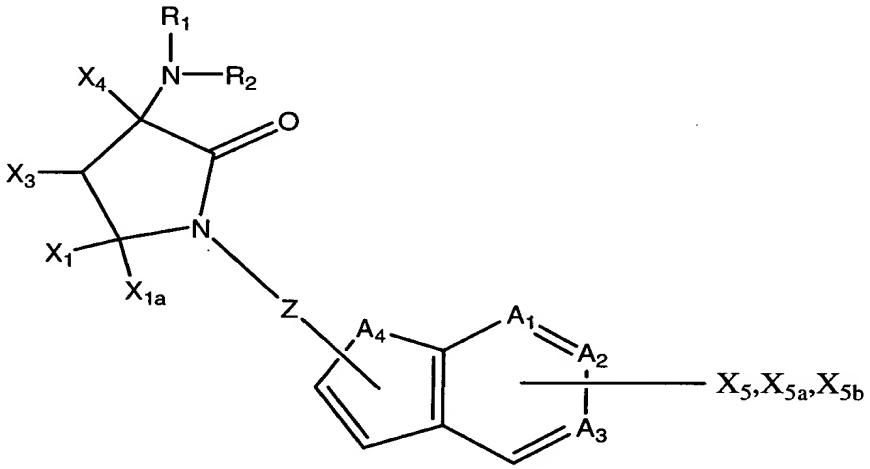
Amendments to the Claims

This listing of claims will replace all prior versions and listings of the claims in the application.

Listing of claims

Claims 1 – 34. (Canceled)

Claim 35. (Currently Amended) ~~The~~ A method ~~of~~ for treating a patient suffering from a physiological disorder capable of being modulated by inhibiting an activity of Factor Xa comprising administering to the patient a therapeutically effective amount of a pyrrolopyridine compound having the formula:



wherein Z is bonded to one of any carbon atom in pyrrolopyridine ring positions 2 to 7, and one of X_5, X_{5a} and X_{5b} is an H, hydroxy, or amino substituent on the ring proximal to Z attachment at a carbon position that is adjacent to the carbon to which Z is attached and another of X_5, X_{5a}, and X_{5b} is a substituent on the ring distal to the carbon to which Z is attached at a position alpha to the nitrogen on the distal ring and is selected from the group consisting of H, hydroxy, H_2N-, (lower alkyl)HN-,wherein the lower alkyl is optionally substituted with an alkyl group substituent, (hydroxy)HN-, (alkoxy)HN- and (amino)HN-, the remaining one of X_5, X_{5a} and X_{5b} is a substituent, as defined below, bonded to any one of the remaining carbon atoms appearing at positions 2 to 7 of the pyrrolopyridine moiety;

one of A_1, A_2 and A_3 is N and the other two are CH;

A_4 is NR_{11} and R_{11} is H, alkyl, aralkyl, heteroaralkyl or $R_8(O)CCH_2$-;

Z is alkylenyl, $-(CH_2)_rC(O)NR"(CH_2)_s$-, $-(CH_2)_sR"NC(O)(CH_2)_r$- or $-(CH_2)_sNR"(CH_2)_r$-, wherein R' and R" are independently: (a) hydrogen; (b) alkyl optionally substituted with one or more alkyl group substituents; (c) aryl, optionally substituted with one or more ring system substituents; (d) heteroaryl, optionally substituted with one or more ring system substituents; (e) aralkenyl, optionally substituted in the aryl portion with one or more ring system substituents and optionally substituted in the alkenyl portion with one or more substituents selected from halogen and cycloalkyl; (f) heteroaralkenyl, optionally substituted in the heteroaryl portion with one or more ring system substituents and optionally substituted in the alkenyl portion with one or more substituents selected from halogen and cycloalkyl; (g) aralkyl, optionally substituted in the aryl portion with one or more ring system substituents and optionally substituted in the alkyl portion with one or more alkyl group substituents; and (h) heteroaralkyl, optionally substituted in the heteroaryl portion with one or more ring system substituents and optionally substituted in the alkyl portion with one or more alkyl group substituents, wherein "r" is selected independently for each occurrence from 1 and 2 and "s" is selected independently for each occurrence from 0, 1, and 2;

R_1 is selected from: (a) hydrogen; (b) alkyl, optionally substituted with one or more alkyl group substituents; (c) alkenyl, optionally substituted with one or more substituents selected from halogen and cycloalkyl ; (d) aralkyl, optionally substituted in the aryl portion with one or more ring system substituents and optionally substituted in the alkyl portion with one or more alkyl group substituents; (e) heteroaralkyl, optionally substituted in the heteroaryl portion with one or more ring system substituents and optionally substituted in the alkyl portion with one or more alkyl group substituents; and (f) a member of the group consisting of $R'O(CH_2)_x$-, $R'O_2C(CH_2)_x$-, $R'C(O)(CH_2)_x$-, $Y^1Y^2NC(O)(CH_2)_x$-, and $Y^1Y^2N(CH_2)_x$-, wherein Y^1 and Y^2 are independently: (a) hydrogen; (b) alkyl, optionally substituted with one or more alkyl group substituents; (c) aryl, optionally substituted with one or more ring system substituents; (d) heteroaryl, optionally substituted with one or more ring system substituents; (e) aralkyl, optionally substituted in the aryl portion with one or more ring system substituents

and optionally substituted in the alkyl portion with one or more alkyl group substituents; and (f) heteroaralkyl, optionally substituted in the heteroaryl portion with one or more ring system substituents and optionally substituted in the alkyl portion with one or more alkyl group substituents, optionally, Y^1 and Y^2 taken together with the N through which Y^1 and Y^2 are linked form a 4 to 7 membered heterocyclyl, R' is as defined above, and x = 1, 2, 3, 4, or 5;

R_2 is selected from: (a) hydrogen; (b) aralkyl, optionally substituted in the aryl portion with one or more ring system substituents and optionally substituted in the alkyl portion with one or more alkyl group substituents; (c) heteroaralkyl, optionally substituted in the heteroaryl portion with one or more ring system substituents and optionally substituted in the alkyl portion with one or more alkyl group substituents; (d) aralkenyl, optionally substituted in the aryl portion with one or more ring system substituents and optionally substituted in the alkenyl portion with one or more substituents selected from halogen and cycloalkyl; (e) heteroaralkenyl, optionally substituted in the heteroaryl portion with one or more ring system substituents and optionally substituted in the alkenyl portion with one or more substituents selected from halogen and cycloalkyl; and (f) a member of the group consisting of $R_3R_4NC(O)(CH_2)_x$-, $R_3S(O)_p$-, ~~or~~ and $R_3R_4NS(O)_p$- wherein: x is selected from 1, 2, 3, 4, and 5 and p is selected independently for each occurrence from 1 and 2;

R_3 is selected from the group consisting of: (a) hydrogen; (b) alkyl, optionally substituted with one or more alkyl group substituents; (c) cycloalkyl, optionally substituted with one or more substituents selected from halogen, methylene, alkyl, fused aryl and fused heteroaryl; (d) heterocyclyl, optionally substituted with with one or more substituents selected from alkyl, halogen, aryl, heteroaryl, fused aryl and fused heteroaryl; (e) aryl, optionally substituted with a ring system substituent; (f) heteroaryl, optionally substituted with a ring system substituent; (g) aralkyl, optionally substituted in the aryl portion with one or more ring system substituents and optionally substituted in the alkyl portion with one or more alkyl group substituents; (h) heteroaralkyl, optionally substituted in the heteroaryl portion with one or more ring system substituents and optionally substituted in the alkyl portion with one or more alkyl group substituents; (i) aralkenyl, optionally substituted in the aryl portion with one

or more ring system substituents and optionally substituted in the alkenyl portion with one or more substituents selected from halogen and cycloalkyl; and (j) heteroaralkenyl, optionally substituted in the heteroaryl portion with one or more ring system substituents and optionally substituted in the alkenyl portion with one or more substituents selected from halogen and cycloalkyl, optionally, ~~or~~ R_1 and R_3 taken together with the -N-S(O)$_p$- moiety or the -N-S(O)$_p$-NR_4- moiety through which R_1 and R_3 are linked form a 5 to 7 membered heterocyclyl optionally substituted with one or more members selected from the group consisting of alkyl, halogen, aryl, heteroaryl, fused aryl, and fused heteroaryl substituents; and

R_4 is selected from the group consisting of: (a) hydrogen; (b) alkyl, optionally substituted with one or more alkyl group substituents (c) cycloalkyl, optionally substituted with one or more substituents selected from halogen, methylene, alkyl, fused aryl and fused heteroaryl; (d) aryl, optionally substituted with a ring system substituent; (e) heteroaryl, optionally substituted with a ring system substituent; (f) aralkyl, optionally substituted in the aryl portion with one or more ring system substituents and optionally substituted in the alkyl portion with one or more alkyl group substituents; (g) heteroaralkyl, optionally substituted in the heteroaryl portion with one or more ring system substituents and optionally substituted in the alkyl portion with one or more alkyl group substituents, optionally R_3 and R_4 taken together with the nitrogen to which R_3 and R_4 are attached form a 4 to 7 membered heterocyclyl, optionally substituted with one or more substituents selected from alkyl, halogen, aryl, heteroaryl, fused aryl, and fused heteroaryl;

X_1 and X_{1a} are independently selected from: (a) H; (b) alkyl, optionally substituted with one or more alkyl group substituents; (c) aryl, optionally substituted with one or more ring system substituents; (d) aralkyl, optionally substituted in the aryl portion with one or more ring system substituents and optionally substituted in the alkyl portion with one or more alkyl group substituents; (e) heteroaryl, optionally substituted with one or more ring system substituents; (f) heteroaralkyl, optionally substituted in the heteroaryl portion with one or more ring system substituents and optionally substituted in the alkyl portion with one or more alkyl group substituents, optionally, X_1 and X_{1a} taken together form oxo;

X_3 is selected from: (a) H; (b) hydroxyl; (c) alkyl, optionally substituted with one or more alkyl group substituents; (d) aryl, optionally substituted with one or more ring system substituents; (e) heteroaryl, optionally substituted with one or more ring system substituents; (f) aralkyl, optionally substituted in the aryl portion with one or more ring system substituents and optionally substituted in the alkyl portion with one or more alkyl group substituents; (g) heteroaralkyl, optionally substituted in the heteroaryl portion with one or more ring system substituents and optionally substituted in the alkyl portion with one or more alkyl group substituents, optionally, X_3 and one of X_1 and X_{1a} taken together form a 4 to 7 membered cycloalkyl;

X_4 is selected from (a) H; (b) alkyl, optionally substituted with one or more alkyl group substituents; and (c) aralkyl, optionally substituted in the aryl portion with one or more ring system substituents and optionally substituted in the alkyl portion with one or more alkyl group substituents;

one of X_5, X_{5a}, and X_{5b} which has not been otherwise selected is selected from H, R_5R_6N-, (hydroxy)HN-, (alkoxy)HN-, or (amino)HN-, R_7O-, R_5R_6NCO-, $R_5R_6NSO_2$-, R_7CO-, halo, cyano, nitro and $R_8(O)CCH_2$-;

R_5 and R_6 are independently selected from (a) H and (b) lower alkyl, optionally substituted with one or more alkyl group substituents; or one of R_5 and R_6 is H and the other is $R_8(O)CCH_2$- or lower acyl;

R_7 is H, lower alkyl optionally substituted with one or more alkyl group substituents or $R_8(O)CCH_2$- ; and

R_8 is selected from H, lower alkyl substituted with one or more alkyl group substituents, alkoxy and hydroxy;

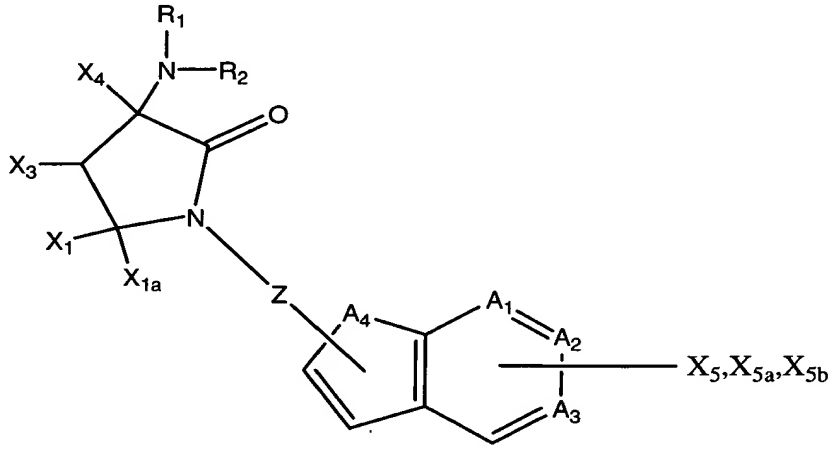
~~claim 1~~ wherein said compound ~~according to claim 1~~ is administered in combination with at least one other agent selected from diagnostic agents, cardioprotective agents, direct thrombin inhibiting agents, anticoagulant agents, antiplatelet agents and fibrinoloytic agents.

Claim 36. (Original) The method of claim 35 wherein said other agent is selected from standard heparin, low molecular weight heparin, direct thrombin inhibitors, aspirin, fibrinogen receptor antagonists, streptokinase, urokinase and tissue plasminogen activator.

Claim 37. (Original) The method of claim 36 wherein said other agent is selected from direct thrombin inhibitors and fibrinogen receptor antagonists.

Claim 38. (Original) The method of claim 37 wherein said thrombin inhibitor is selected from boroarginine derivatives, boropeptides, hirudin, argatroban and the pharmaceutically acceptable salts, prodrugs, derivatives and analogs thereof.

Claim 39. (Currently Amended) ~~The~~ A pharmaceutical composition comprising a pharmaceutically acceptable carrier and pharmaceutically acceptable amount of a pyrrolopyridine compound having the formula:



wherein Z is bonded to one of any carbon atom in pyrrolopyridine ring positions 2 to 7, and one of X_5, X_{5a} and X_{5b} is an H, hydroxy, or amino substituent on the ring proximal to Z attachment at a carbon position that is adjacent to the carbon to which Z is attached and another of X_5, X_{5a}, and X_{5b} is a substituent on the ring distal to the carbon to which Z is

attached at a position alpha to the nitrogen on the distal ring and is selected from the group consisting of H, hydroxy, H_2N-, (lower alkyl)HN-,wherein the lower alkyl is optionally substituted with an alkyl group substituent, (hydroxy)HN-, (alkoxy)HN- and (amino)HN-, the remaining one of X_5, X_{5a} and X_{5b} is a substituent, as defined below, bonded to any one of the remaining carbon atoms appearing at positions 2 to 7 of the pyrrolopyridine moiety;

one of A_1, A_2 and A_3 is N and the other two are CH;

A_4 is NR_{11} and R_{11} is H, alkyl, aralkyl, heteroaralkyl or $R_8(O)CCH_2$-;

Z is alkylenyl, $-(CH_2)_rC(O)NR''(CH_2)_s-$, $-(CH_2)_sR''NC(O)(CH_2)_r-$ or $-(CH_2)_sNR''(CH_2)_r-$, wherein R' and R" are independently: (a) hydrogen; (b) alkyl optionally substituted with one or more alkyl group substituents; (c) aryl, optionally substituted with one or more ring system substituents; (d) heteroaryl, optionally substituted with one or more ring system substituents; (e) aralkenyl, optionally substituted in the aryl portion with one or more ring system substituents and optionally substituted in the alkenyl portion with one or more substituents selected from halogen and cycloalkyl; (f) heteroaralkenyl, optionally substituted in the heteroaryl portion with one or more ring system substituents and optionally substituted in the alkenyl portion with one or more substituents selected from halogen and cycloalkyl; (g) aralkyl, optionally substituted in the aryl portion with one or more ring system substituents and optionally substituted in the alkyl portion with one or more alkyl group substituents; and (h) heteroaralkyl, optionally substituted in the heteroaryl portion with one or more ring system substituents and optionally substituted in the alkyl portion with one or more alkyl group substituents, wherein "r" is selected independently for each occurrence from 1 and 2 and "s" is selected independently for each occurrence from 0, 1, and 2;

R_1 is selected from: (a) hydrogen; (b) alkyl, optionally substituted with one or more alkyl group substituents; (c) alkenyl, optionally substituted with one or more substituents selected from halogen and cycloalkyl ; (d) aralkyl, optionally substituted in the aryl portion with one or more ring system substituents and optionally substituted in the alkyl portion with

one or more alkyl group substituents; (e) heteroaralkyl, optionally substituted in the heteroaryl portion with one or more ring system substituents and optionally substituted in the alkyl portion with one or more alkyl group substituents; and (f) a member of the group consisting of $R'O(CH_2)_x$-, $R'O_2C(CH_2)_x$-, $R'C(O)(CH_2)_x$-, $Y^1Y^2NC(O)(CH_2)_x$-, and $Y^1Y^2N(CH_2)_x$-, wherein Y^1 and Y^2 are independently: (a) hydrogen; (b) alkyl, optionally substituted with one or more alkyl group substituents; (c) aryl, optionally substituted with one or more ring system substituents; (d) heteroaryl, optionally substituted with one or more ring system substituents; (e) aralkyl, optionally substituted in the aryl portion with one or more ring system substituents and optionally substituted in the alkyl portion with one or more alkyl group substituents; and (f) heteroaralkyl, optionally substituted in the heteroaryl portion with one or more ring system substituents and optionally substituted in the alkyl portion with one or more alkyl group substituents, optionally, Y^1 and Y^2 taken together with the N through which Y^1 and Y^2 are linked form a 4 to 7 membered heterocyclyl, R' is as defined above, and x = 1, 2, 3, 4, or 5;

R_2 is selected from: (a) hydrogen; (b) aralkyl, optionally substituted in the aryl portion with one or more ring system substituents and optionally substituted in the alkyl portion with one or more alkyl group substituents; (c) heteroaralkyl, optionally substituted in the heteroaryl portion with one or more ring system substituents and optionally substituted in the alkyl portion with one or more alkyl group substituents; (d) aralkenyl, optionally substituted in the aryl portion with one or more ring system substituents and optionally substituted in the alkenyl portion with one or more substituents selected from halogen and cycloalkyl; (e) heteroaralkenyl, optionally substituted in the heteroaryl portion with one or more ring system substituents and optionally substituted in the alkenyl portion with one or more substituents selected from halogen and cycloalkyl; and (f) a member of the group consisting of $R_3R_4NC(O)(CH_2)_x$-, $R_3S(O)_p$-, ~~or~~ and $R_3R_4NS(O)_p$- wherein: x is selected from 1, 2, 3, 4, and 5 and p is selected independently for each occurrence from 1 and 2;

R_3 is selected from the group consisting of: (a) hydrogen; (b) alkyl, optionally substituted with one or more alkyl group substituents; (c) cycloalkyl, optionally substituted with one or more substituents selected from halogen, methylene, alkyl, fused aryl and fused

heteroaryl; (d) heterocyclyl, optionally substituted with with one or more substituents selected from alkyl, halogen, aryl, heteroaryl, fused aryl and fused heteroaryl; (e) aryl, optionally substituted with a ring system substituent; (f) heteroaryl, optionally substituted with a ring system substituent; (g) aralkyl, optionally substituted in the aryl portion with one or more ring system substituents and optionally substituted in the alkyl portion with one or more alkyl group substituents; (h) heteroaralkyl, optionally substituted in the heteroaryl portion with one or more ring system substituents and optionally substituted in the alkyl portion with one or more alkyl group substituents; (i) aralkenyl, optionally substituted in the aryl portion with one or more ring system substituents and optionally substituted in the alkenyl portion with one or more substituents selected from halogen and cycloalkyl; and (j) heteroaralkenyl, optionally substituted in the heteroaryl portion with one or more ring system substituents and optionally substituted in the alkenyl portion with one or more substituents selected from halogen and cycloalkyl, optionally, ~~or~~ R_1 and R_3 taken together with the -N-S(O)$_p$- moiety or the -N-S(O)$_p$-NR_4- moiety through which R_1 and R_3 are linked form a 5 to 7 membered heterocyclyl optionally substituted with one or more members selected from the group consisting of alkyl, halogen, aryl, heteroaryl, fused aryl, and fused heteroaryl substituents; and

R_4 is selected from the group consisting of: (a) hydrogen; (b) alkyl, optionally substituted with one or more alkyl group substituents (c) cycloalkyl, optionally substituted with one or more substituents selected from halogen, methylene, alkyl, fused aryl and fused heteroaryl; (d) aryl, optionally substituted with a ring system substituent; (e) heteroaryl, optionally substituted with a ring system substituent; (f) aralkyl, optionally substituted in the aryl portion with one or more ring system substituents and optionally substituted in the alkyl portion with one or more alkyl group substituents; (g) heteroaralkyl, optionally substituted in the heteroaryl portion with one or more ring system substituents and optionally substituted in the alkyl portion with one or more alkyl group substituents, optionally R_3 and R_4 taken together with the nitrogen to which R_3 and R_4 are attached form a 4 to 7 membered heterocyclyl, optionally substituted with one or more substituents selected from alkyl, halogen, aryl, heteroaryl, fused aryl, and fused heteroaryl;

X_1 and X_{1a} are independently selected from: (a) H; (b) alkyl, optionally substituted with one or more alkyl group substituents; (c) aryl, optionally substituted with one or more ring system substituents; (d) aralkyl, optionally substituted in the aryl portion with one or more ring system substituents and optionally substituted in the alkyl portion with one or more alkyl group substituents; (e) heteroaryl, optionally substituted with one or more ring system substituents; (f) heteroaralkyl, optionally substituted in the heteroaryl portion with one or more ring system substituents and optionally substituted in the alkyl portion with one or more alkyl group substituents, optionally, X_1 and X_{1a} taken together form oxo;

X_3 is selected from: (a) H; (b) hydroxyl; (c) alkyl, optionally substituted with one or more alkyl group substituents; (d) aryl, optionally substituted with one or more ring system substituents; (e) heteroaryl, optionally substituted with one or more ring system substituents; (f) aralkyl, optionally substituted in the aryl portion with one or more ring system substituents and optionally substituted in the alkyl portion with one or more alkyl group substituents; (g) heteroaralkyl, optionally substituted in the heteroaryl portion with one or more ring system substituents and optionally substituted in the alkyl portion with one or more alkyl group substituents, optionally, X_3 and one of X_1 and X_{1a} taken together form a 4 to 7 membered cycloalkyl;

X_4 is selected from (a) H; (b) alkyl, optionally substituted with one or more alkyl group substituents; and (c) aralkyl, optionally substituted in the aryl portion with one or more ring system substituents and optionally substituted in the alkyl portion with one or more alkyl group substituents;

one of X_5, X_{5a}, and X_{5b} which has not been otherwise selected is selected from H, R_5R_6N-, (hydroxy)HN-, (alkoxy)HN-, or (amino)HN-, R_7O-, R_5R_6NCO-, $R_5R_6NSO_2$-, R_7CO-, halo, cyano, nitro and $R_8(O)CCH_2$-;

R_5 and R_6 are independently selected from (a) H and (b) lower alkyl, optionally substituted with one or more alkyl group substituents; or one of R_5 and R_6 is H and the other is $R_8(O)CCH_2$- or lower acyl;

R_7 is H, lower alkyl optionally substituted with one or more alkyl group substituents or $R_8(O)CCH_2$- ; and

R_8 is selected from H, lower alkyl substituted with one or more alkyl group substituents, alkoxy and hydroxy;

~~of claim 30~~ and further comprising at least one other agent selected from diagnostic agents, cardioprotective agents, direct thrombin inhibiting agents, anticoagulant agents, antiplatelet agents and fibrinoloytic agents.

Claim 40. (Original) The pharmaceutical composition of claim 39 wherein said other agent is selected from standard heparin, low molecular weight heparin, direct thrombin inhibitors, aspirin, fibrinogen receptor antagonists, streptokinase, urokinase and tissue plasminogen activator.

Claim 41. (Original) The pharmaceutical composition of claim 40 wherein said other agent is selected from direct thrombin inhibitors and fibrinogen receptor antagonists.

Claim 42. (Cancelled)